Chlordane

CHLORDANE

International Programme on Chemical Safety
Poisons Information Monograph 574
Chemical

1. NAME

1.1 Substance

Chlordane

1.2 Group

Chlorinated "cyclodiene" insecticide

1.3 Synonyms

Aspon;
Belt;
CD 68;
Chlorindan;
Chlorkil;
Corodan;
Cortilon neu;
Dowchlor;
HCS 3260;
Kypchlor;
M 140;
Niran;

Octachlor;
Octoterr;
Ortho-Klor;
Synklor;
Tat-Chlor 4;
Topichlor;
Toxichlor;
Velsicol-1068.

1.4 Identification numbers

1.4.1 CAS number

57-74-9

1.4.2 Other numbers

RTECS	PB9800000
ICSC	0740
UN	2996
EC	602-047-00-8
NCI	8931
Standard Transportation Number	49 131 70
EPA Hazardous Waste Number	UO36
DOT ID & Guide	2762 131
Transport Emergency Card:	TEC(R)-61G41c
Chlordane [technical grade]	CAS12789-03-6
cis-Chlordane	CAS12789-03-6
trans-Chlordane	CAS 5103-74-2
gamma-Chlordane	CAS 5566-34-7

1.5 Main brand names, Main trade names

Belt;
Corodane;
Chlortox;
Niran;
Octachlor;
Octa-Klor;
Sym-klor;
Toxichlor.

1.6 Main manufacturers, main importers

Velsicol Chemical Corp.

2. SUMMARY

2.1 Main risks and target organs

Chlordane is a central nervous system stimulant. The liver and the kidney are the other organs significantly affected by chlordane.

2.2 Summary of clinical effects

Poisoning by the chlordane and other cyclodiene

insecticides is more likely to begin with the sudden onset of convulsions preceeded by vomiting. Seizures caused by cyclodienes may appear as long as 48 hours after exposure, and then may recur periodically over several days following the initial episode. Tonic-clonic convulsions usually are accompanied by confusion, incoordination, excitability, or, in some instances coma and hypotension. Respiratory failure may also occur.

2.3 Diagnosis

The diagnosis is based on the history of exposure (dermal, inhalational or gastrointestinal) and signs of central nervous system hyperexcitability including seizures.

Blood levels are not clinically useful, but could help to confirm the exposure. Treatment will be determined by clinical status.

Analysis is difficult because of the complex nature of chlordane. The principal method for its qualitative and quantitative determination is gas-liquid chromatography with electron capture detection.

2.4 First aid measures and management principles

Treatment is symptomatic. It is aimed at controlling convulsions, coma, and respiratory depression. Cardio-vascular function must be observed.

To control convulsions use clonazepam IV or diazepam IV or per rectum. Intravenous barbiturates may also be used.Once convulsions are controlled further treatment with *Phenytoin* or *Sodium Valproate* should be continued as long as required.

Do not give fats, oils or milk since these will enhance absorption from the intestinal tract.

If the patient is conscious, and a large quantity of chlordane has been ingested not more than one hour ago perform gastric lavage only after tracheal intubation. This should be followed by intragastic administration of a large amount of activated charcoal slurry and a laxative.

In the case of skin contact remove and discard contaminated clothing and wash exposed skin including hair and nails with (soap and) copious amounts of water,.

Opiates and *adrenaline* and *nor-adrenaline* should only be given with extreme caution. *Aminophylline, atropine* or *oily laxatives* should not be administered.

Rescuers must take precautions to avoid personal exposure.

3. PHYSICOCHEMICAL PROPERTIES

3.1 Origin of the substance

A synthetic product (Budavari et al., 1996).

3.2 Chemical structure

Structural names

1,2,4,5,6,7,8,8-octachloro-2,3,3a,4,7,7a-hexahydro-4,7-methanoindene (IUPAC)

1,2,4,5,6,7,8,8-octachloro-3a,4,7,7a-tetrahydro-4,7-methanoindane
1,2,4,5,6,7,8,8-=octachloro-2,3,3a,4,7,7a-hexahydro-4,7-methano-1 H-indene
Structural formula

Molecular formula $C_{10}H_6Cl_8$
Molecular weight 409.8

3.3 Physical properties

3.3.1 Colour

Amber

3.3.2 State/Form

Liquid-viscous fluid

3.3.3 Description

Technical chlordane is a viscous, amber coloured liquid.

It has a pungent, chlorine like odor (NIOSH, 1998)

Solubility: It is insoluble in water but soluble in most organic solvents including acetone, cyclohexanone, ethanol, deodorized kerosene, isopropanol, trichloroethylene (Tomlin, 1994).

Boiling point at 0.27 kPa: 175 °C (IPCS/CEC, 1999)

Melting point: 103 to 105 °C (IPCS, 1988)

Relative density (water=1): 1.59-1.63 (Budavari et al., 1996)

Vapour pressure, Pa at 25 °C: 0.0013 (IPCS/CEC, 1999)

Octanol/water partition coefficient as log Pow: 2.78

(IPCS/CEC, 1999)

Viscosity 69 Poises at 25 °C (Budavari et al., 1996)

3.4 Hazardous characteristics

The substance decomposes on heating and/or on burning and on contact with bases producing toxic fumes including chlorine, hydrogen chloride, and phosgene. Attacks iron, zinc, plastics, rubber and coatings (IPCS/CEC, 1999).

Above 56 °C explosive vapor/air mixtures may be formed. Explosion hazard will depend on the solvent used or on the characteristics of the dust.

4. USES

4.1 Uses

4.1.1 Uses

Pesticide for use against invertebrate animals

4.1.2 Description

Chlordane is a persistent, non-systemic, contact and ingested insecticide with some fumigant action. It is used on land against formicidae, coleoptera, noctuidae larvae, saltatoria, subterranean termites (including Coptotermes spp.) and many other insect pests. It also controls household insects, pests of man and domestic animals, is used as a wood preservative, a protective treatment for underground cables and to reduce earthworm populations in lawns. It may be applied to soil, directly to foliage or as a seed treatment (Tomlin, 1994).

All U.S registrations of chlordane have been cancelled (Reigart & Roberts, 1999).

Chlordane is on list of 12 persistent organochlorine pesticides (POP) identified by UNEP Governing Council, for which international action is required to reduce the risks to human health and the environment. It is also subject to the prior informed consent procedure of UNEP and FAO.

4.2 High risk circumstance of poisoning

Accidental poisoning can occur in children by chlordane stored in the home or garage.

Accidental exposure can occur among formulating plant workers.

Suicide attempts.

Exposure of the general population may occur in dwellings treated with chlordane for termite control.

Individuals with a history of convulsive disorders would be expected to be at increased risk from exposure (Mackison et al., 1981).

4.3 Occupationally exposed populations

Factory workers involved in syntheses of chlordane,workers involved in formulating and dispensing chlordane and public health workers involved in pest control.

5. ROUTES OF EXPOSURE

5.1 Oral

Ingestion occurs through accidental or deliberate ingestion or accidental ingestion of contaminated foodstuffs.

5.2 Inhalation

Chlordane vapor is absorbed by inhalation.

5.3 Dermal

Chlordane is readily absorbed after dermal contact, and the absorption is variable depending on the type on the type of solvent used.

5.4 Eye

Exposure to vapors, dust and aerosols.

5.5 Parenteral

No data available.

5.6 Other

No data available

6. KINETICS

6.1 Absorption by route of exposure

In studies on 4 male rabbits, a combination of ^{14}C-alpha and gamma-chlordane (app. 1700 mg of each, administered orally in 4 doses at 4-day intervals), was well absorbed (Balba & Saha, 1978). Rats that breathed [^{14}C] chlordane vapor for 30 min retained 77% of the total inhaled (Stubbfield & Dorough, 1979).

6.2 Distribution by route of exposure

Studies using radio-labelled chlordane showed that after oral administration, the radioactivity was well distributed in tissues of rats (Barnett & Dorough, 1974) and rabbits (Balba & Saha, 1978). Rats, whether being treated with single oral doses of chlordane or fed diets containing this compound, retained the highest levels of residues in adipose tissue, followed by the liver, kidney, brain and muscle. More of the gamma-isomer was retained than of the alpha isomer. The tissue distribution of chlordane in rabbits was found to be similar to that in rats (Poonawalla & Korte, 1971; Balba & Saha, 1978).

Human milk samples obtained from 1436 women residing in United States were analyzed by GLC . While chlordane was not detected in any of the milk samples, its metabolite oxychlordane was found above the detection limit (95.8 ppb) in 74% of the samples (Savage et al., 1981).

6.3 Biological halflife by route of exposure

Serum half-life of 88 days was reported in one child (Aldrich & Holmes, 1969). In another study, a half-life of 34 days for the elimination of chlordane was calculated from kinetic studies of a patient who accidentally consumed a chlordane-containing pesticide (Olanoff et al., 1983).

6.4 Metabolism

Chlordane is metabolized very slowly (Gosselin et al., 1984). Most metabolites of chlordane are far less toxic than the parent material, but oxychlordane is more toxic with a LD_{50} in rats of 19.1 mg/kg (FAO/WHO, 1971).

In vivo and in vitro studies in rats have revealed two routes of biotransformation of chlordane and shown that the metabolites include trans-chlordane, 1,2,-didichlorochlordene, oxychlordane, 1-hydroxy-2-chloro-2,3-epoxychlordene, chlordene chlorohydrin, and 1,2-trans-dihydroxydihydrochlordene, as well as metabolites of heptachlor (Tashiro & Matsumura, 1977; Briemfield & Street 1979). In vitro studies showed that the livers of rat and humans had almost identical ability to degrade chlordane, except that human liver has little capacity to convert trans-nonachlor to trans-chlordane. This is consistent with the accumulation of trans-nonachlor in people but not in rats (Tashiro & Matsumura, 1978).

6.5 Elimination and excretion

Chlordane is excreted primarily in the faeces (Poonawalla & Korte, 1971).

Elimination of radiolabelled chlordane (3:1 alpha- and gamma-chlordane) and the individual isomers was studied in rats. Single oral doses of 0.05, 0.2 and 1 mg/kg body weight

in corn oil were almost completely eliminated after 7 days; 24 hours after administration, 70 % of alpha- chlordane and 60 % of the gamma-isomer were excreted. Female rats excreted more of the dose in the urine than the males (Barnett & Dorough, 1974).

7. TOXICOLOGY

7.1 Mode of action

Chlorinated hydrocarbon insecticides act by altering the electrophysiological and associated enzymatic properties of nerve cell membranes, causing a change in the kinetics of Na+ and K+ ion flow through the membrane. Disturbances of calcium transport of Ca+2-ATPase activity may also be involved, as well as phosphokinase activities (Hayes & Laws, 1991).

The cyclodiene compounds antagonize the action of the neurotransmitter (-aminobutyric acid (GABA), which induces the uptake of chloride ions by neurons. The blockage of this activity by cyclodiene insecticides results in only partial repolarization of the neuron and a state of uncontrolled excitation (Klassen & Watkins, 1999).

7.2 Toxicity

7.2.1 Human data

7.2.1.1 Adults

Chlordane has not been a common substance causing poisoning. All established cases have been associated with gross exposure. In most instances, including those with full recovery, convulsions appeared within 0.5 to 3 hours after ingestion (Micks, 1954; Curley & Garretson, 1969; Aldrich & Holmes, 1969) or after dermal exposure involving spillage.

During an acute episode, a man experienced a brief episode of oliguria with proteinuria, hematuria and mild hypertension, all of which returned to normal (Stranger & Kerridge, 1968)

One 30-year-old woman was exposed to chlordane through carelessness and overuse over a 1 to 4 week period. Myoclonic jerks occurred only after a delay of a month, although the patient previously suffered from circumoral numbness, anorexia, nausea and fatigue (Garretson et al., 1985). Malaise and anorexia became the dominant symptoms for 6 months before treatment. Dysfunctional bleeding was attributed to hepatic enzyme

induction by the chlordane and increased metabolism of contraceptive medication.

In an episode of contamination of a public water supply by chlordane (probably intentional) many people were affected and the water level in a residence near the point of intake was 6.600 ppm. Although chlordane, its contaminants, or its metabolites were not detected in residents, a significant proportion reported gastrointestinal symptoms, skin and eye irritation and headaches (Morbidity and Mortality Weekly Reports, 1981).

Two cases of chlordane poisoning were reported in 1955. One was caused by absorption of accidentally spilled chlordane, 40 minutes later the victim became confused and suddenly began having convulsions. She was dead on arrival to the physician's office. The other was a suicide attempt where the individual (female) swallowed 6 g of chlordane (104 mg/kg body weight) and died 9´ days after the incident (Derbes et al., 1955).

One man occupationally exposed to chlordane developed episodes of paresthesia and later twitching of the right hand and arm. Additional episodes, beginning in the same way, ended as grand mal convulsions followed by unconsciousness. He has recovered without treatment when he discontinued contact with chlordane.

Topical skin application of about 30 g to an adult resulted in death in 40 minutes (ACGIH, 1986).

The acute lethal dose for man is estimated to be 25 to 50 mg/kg body weight (IPCS, 1984).

7.2.1.2 Children

A 15-month-old girl ingested a mouthful of chlordane suspension and after 3 hours, displayed tremors and incoordination (Lensky & Evans, 1952). Repeated seizures developed and she was treated with ethyl chloride, amobarbital and gastric lavage with magnesium sulfate. The child recovered completely and ataxia and excitability disappeared after 2 to 3 weeks. At 26 years of age, she was in excellent health and

appeared not to suffer any consequences from the childhood episode (Taylor et al., 1979).

A 2-year-old child had drunk an unknown amount of a 74% formulation of chlordane (Curley & Garretson, 1969). Vomiting preceded convulsions, which were controlled by phenobarbital; the EEG pattern was normal within 40 hours and the child recovered.

A similar poisoning incident was observed with a 4-year-old child (Aldridge & Homes, 1969). Convulsions were treated with phenobarbital and the individual recovered.

After a 21-month-old child who had typical convulsions following ingestion of an unknown number of chlordane pellets recovered; she had albuminuria and a positive urine culture; to what extent chlordane may have influenced the renal tract infection was unclear (Canada, 1962).

7.2.2 Relevant animal data

Acute oral LD_{50} for rats 460 mg/kg (IPCS, 1998)

Acute oral LD_{50} for mice 430 mg/kg

Acute oral LD_{50} for rabbits 300 mg/kg

Acute percutaneous LD_{50} for rabbits >200 but <2000 mg/kg (Tomlin, 1994), extremely irritating to their eyes but produces only mild irritant to their skin.

Inhalation LC_{50} (4 hour) (for exposure to an aerosol, nominal concentration) >200 mg/L

NOEL for dogs 3 mg/kg diet.

7.2.3 Relevant in vitro data

Sufficient human data are available

7.2.4 Workplace standards

OSHA PEL TWA0.5 mg/m^3 (skin)

TLV0.5 mg/m^3 (as TWA) (ACGIH 1999)

NIOSH REL Ca TWA 0.5 mg/m^3 skin

NIOSH IDLH Potential occupational carcinogen

100 mg/m^3

7.2.5 Acceptable daily intake (ADI)

ADI 0.0005 mg/kg (IPCS, 1997)

7.3 Carcinogenicity

Case reports of leukaemia and other blood dyscrasias have been associated with exposure to chlordane/heptachlor, primarily in domestic situations (Furie & Trubowitz,1976).

Mortality from lung cancer was slightly elevated in two cohort studies of pesticide applicators; and one of chlordane/heptachlor manufacturers. Termite control operators probably have greater exposure to chlordane than other pesticide applicators. However, in one study of applicators, the excess occurred only among workers who were not engaged in termite control (Mac Mahon et al., 1988). In the other study of applicators, the relative risk for lung cancer among workers engaged in termite control was similar to that of workers engaged in other pest control. Inconsistencies in these findings make it difficult to ascribe the excesses to exposure to chlordane.

Small excess risks for other cancers, including leukaemia, non-Hodgkin's lymphoma and soft tissue sarcoma and cancers of the brain, skin, bladder and stomach were observed, with little consistency among studies (IARC, 1991).

Chlordane, technical-grade chlordane, heptachlor, technical-grade heptachlor, heptachlorepoxide and a mixture of heptachlor and heptachlorepoxide have been tested for carcinogenicity by oral administration in several strains of mice and rats. These studies uniformly demonstrate increases of hepatocellular neoplasms in mice of each sex. Increases in the incidence of thyroid follicular-cell neoplasms were observed in rats treated with chlordane and technical-grade heptachlor. An increased incidence of malignant fibrous histiocytomas was observed in one study in male rats treated with chlordane. A small increase in the incidence of liver adenomas was seen in one study in male rats treated with technical grade chlordane.

Chlordane has been evaluated by the International Agency for Research on Cancer (IARC, 1979; 1987; 1991). It was concluded that there is inadequate evidence in humans for the carcinogenicity of chlordane and sufficient evidence in experimental animals for the carcinogenicity of chlordane. The overall evaluation of IARC on chlordane is Group 2B (possibly carcinogenic to humans).

7.4 Teratogenicity

No evidence of teratogenicity was found in animal

studies (IPCS, 1984).

7.5 Mutagenicity

Alpha-chlordane, gamma chlordane and chlordene were tested in the Ames Salmonella microsome assay and were not mutagenic (Simon et al., 1977). Chlordane was not mutagenic when tested using 5 different strains of Salmonella typhimurium in the Ames assay (Ergovich & Rachid, 1977).

More studies on animal and human cells in culture have shown that chlordane is not mutagenic or is only weakly mutagenic (Williams, 1979; Maslansky & Williams, 1981; Tong et al., 1981). Further work by Telang et al. (1982) showed that chlordane, was not mutagenic to an adult rat liver cell line but inhibited cell to cell communication in a rat liver 6-thioguanine resistant sensitive cell line.

Chlordane and heptachlor did not cause dominant lethal effects in mice. Both compounds inhibited gap-junctional intercellular communication and induced gene mutations in rodent cells but did not induced unscheduled DNA synthesis. Neither chlordane nor heptachlor was mutagenic to bacteria and neither of these damaged bacterial or plasmid DNA (IARC, 1991).

7.6 Interactions

Chlordane has been shown to exert a protective effect against several organophosphorus and carbamate insecticides (Williams, 1967; Street, 1969; Williams 1970).

Protein deficiency has been shown to double the acute toxicity of chlordane in rats (Boyd, 1972). Chlordane has also shown to increase the hepatotoxic effects of carbon tetrachloride in the rat (Stenger et al., 1975;Mahon, 1977; 1979).

8. TOXICOLOGICAL ANALYSES AND BIOMEDICAL INVESTIGATIONS

8.1 Material sampling plan

8.1.1 Sampling and specimen collection

8.1.1.1 Toxicological analyses

8.1.1.2 Biomedical analyses

8.1.1.3 Arterial blood gas analysis

8.1.1.4 Haematological analyses

8.1.1.5 Other (unspecified) analyses

8.1.2 Storage of laboratory samples and specimens

8.1.2.1 Toxicological analyses

8.1.2.2 Biomedical analyses

8.1.2.3 Arterial blood gas analysis

8.1.2.4 Haematological analyses

8.1.2.5 Other (unspecified) analyses

8.1.3 Transport of laboratory samples and specimens

8.1.3.1 Toxicological analyses

8.1.3.2 Biomedical analyses

8.1.3.3 Arterial blood gas analysis

8.1.3.4 Haematological analyses

8.1.3.5 Other (unspecified) analyses

8.2 Toxicological Analyses and Their Interpretation

8.2.1 Tests on toxic ingredient(s) of material

8.2.1.1 Simple Qualitative Test(s)

8.2.1.2 Advanced Qualitative Confirmation Test(s)

8.2.1.3 Simple Quantitative Method(s)

8.2.1.4 Advanced Quantitative Method(s)

8.2.2 Tests for biological specimens

8.2.2.1 Simple Qualitative Test(s)

8.2.2.2 Advanced Qualitative Confirmation Test(s)

8.2.2.3 Simple Quantitative Method(s)

8.2.2.4 Advanced Quantitative Method(s)

8.2.2.5 Other Dedicated Method(s)

8.2.3 Interpretation of toxicological analyses

8.3 Biomedical investigations and their interpretation

8.3.1 Biochemical analysis

8.3.1.1 Blood, plasma or serum

"Basic analyses"

"Dedicated analyses"

"Optional analyses"

8.3.1.2 Urine

"Basic analyses"

"Dedicated analyses"

"Optional analyses"

8.3.1.3 Other fluids

8.3.2 Arterial blood gas analyses

8.3.3 Haematological analyses

"Basic analyses"

"Dedicated analyses"

"Optional analyses"

8.3.4 Interpretation of biomedical investigations

8.4 Other biomedical (diagnostic) investigations and their interpretation

8.5 Overall interpretation of all toxicological analyses and toxicological investigations

8.6 References

9. CLINICAL EFFECTS

9.1 Acute poisoning

9.1.1 Ingestion

Following ingestion of chlordane some patients have experienced nausea and vomiting before signs of central nervous system overactivity appeared. However a convulsive fit could be the first clear indication of illness. Convulsions often last about a minute and may recur at intervals of about 5 minutes. Convulsions usually are accompanied by confusion, incoordination, excitability, or in some instances, coma. Respiratory failure may also occur (Olanoff et al., 1983).

9.1.2 Inhalation

Chlordane may be absorbed by inhalation. Symptoms are basically the same as by ingestion.

9.1.3 Skin exposure

Skin is a significant route of exposure, and

may even result in death (ACGIH, 1986). Symptoms are basically the same as by ingestion.

9.1.4 Eye contact

Contact with the eyes may cause ocular irritation and pain (IPCS, CEC, 1999).

9.1.5 Parenteral exposure

No data available.

9.1.6 Other

Symptoms were relatively mild in a poisoning by rectally administered chlordane involving a dose of 0.53 to 1.9 mg/kg (Marquart, 1982).

9.2 Chronic poisoning

9.2.1 Ingestion

No data available.

9.2.2 Inhalation

No data available

9.2.3 Skin exposure

No data available

9.2.4 Eye contact

No data available

9.2.5 Parenteral exposure

No data available

9.2.6 Other

Recent evidence indicates that neurotoxicity, a known human endpoint in acute exposures may be a relevant endpoint in chronic human exposures. No chronic animal studies have examined neurotoxicity (Kilburn & Thornton, 1995).

9.3 Course, prognosis, cause of death

Typical, serious poisoning by chlordane is characterized by onset of violent convulsions within 0.5 to 3 hours, and either death or the start of recovery within a few hours to a day (Hayes & Laws, 1991). Seizures caused by chlordane may appear as long as 48 hours after exposure, and then may recur periodically over several days following the initial episode (Reigart & Roberts, 1999). Nausea and vomiting may occur

before signs of central nervous system activity have appeared. Convulsions may and may not be the first clear indication of illness. Convulsions usually are accompanied by confusion, incoordination, excitability, or, in some instances, coma. Respiratory failure may also occur (Olanoff et al., 1983). Death may follow respiratory failure (IPCS, 1984).

9.4 Systematic description of clinical effects

9.4.1 Cardiovascular

Arrhythmias may occur owing to myocardial sensitivity to catecholamines (Olson, 1999).

9.4.2 Respiratory

The effects of chlordane on the respiratory system are secondary to the effects on the nervous system (Hayes & Laws, 1991).

9.4.3 Neurological

9.4.3.1 Central nervous system (CNS)

Central nervous system excitation is the primary toxic effect seen in humans. Convulsions can occur suddenly after a massive overdose. Convulsions often last about a minute and may recur at intervals of about 5 min. Convulsions usually are accompanied by confusion, incoordination, excitability, or, in some instances, coma.

9.4.3.2 Peripheral nervous system

Paraesthesia of the extremities has been reported in a man accidentally exposed to chlordane (Barnes, 1967).

9.4.3.3 Autonomic nervous system

No data available.

9.4.3.4 Skeletal and smooth muscle

Rhabdomyolysis may occur.

9.4.4 Gastrointestinal

Nausea and vomit may occur.

9.4.5 Hepatic

Chlordane is a potent inducer of hepatic microsomal enzymes (Hart et al., 1963).

9.4.6 Urinary

9.4.6.1 Renal

After ingestion, renal injury may develop (Olson, 1999).

9.4.6.2 Other

No data available.

9.4.7 Endocrine and reproductive systems

Induction of hepatic microsomal enzymes may result in hormonal disturbances because of accelerated metabolism of endogenous steroids (Street et al., 1969).

At concentrations above 30 mg per kg of fodder, chlordane interferes with reproduction in rats and mice (IPCS, 1988).

No multi-generational reproductive studies, by any route, exist for technical chlordane. Several items within the current chlordane database suggest that reproductive effects could be a relevant endpoint for chlordane. The study of Cassidy et al. (1994) indicates alterations in reproductive-related behaviour in male rats as a consequence of chlordane exposure.

Accumulation of a major component of a technical chlordane (heptachlor) in ovary, uterus and adrenals in non-pregnant rats within 30 after an oral dose of 120 mg/kg heptachlor. In pregnant rats, levels were markedly elevated in the uterus compared to non-pregnant rats; the higher accumulation is believed to be a result of a slower metabolic turnover of heptachlor. These results indicate that chlordane or some of its components/metabolites have an increased affinity towards reproductive organs during pregnancy and may have potential to adversely affect reproductive processes (Rani et al., 1992).

9.4.8 Dermatological

Skin irritation results from extensive contact with organochlorine pesticides or with the white petroleum distillate vehicles.

9.4.9 Eye, ear, nose, throat: local effects

May cause redness and pain in the eyes (IPCS/CEC, 1999).

9.4.10 Haematological

Case reports of leukaemia and other blood dyscrasias have been associated exposure to chlordane. The bone marrow showing evidence of dyserythropoiesis, eosinophilia and megaloblastosis was reported after extensive exposure with recovery after 4 months (Furie, 1976)

9.4.11 Immunological

Altered immune competence was reported in the offspring off mice whose mothers had received chlordane at a rate of 8.0 mg/kg/day throughout gestation but not in young whose mothers received 0.16 mg/kg/day (Cranmer et. al., 1979, Spyker-Cranmer et al., 1982).

9.4.12 Metabolic

9.4.12.1 Acid-base disturbances

Metabolic acidosis may occur.

9.4.12.2 Fluid and electrolyte disturbances

No data available

9.4.12.3 Others

No data available

9.4.13 Allergic reactions

No data available

9.4.14 Other clinical effects

9.4.15 Special risks

Pregnancy

In one study with rats, chlordane or some of its components/metabolites show an increased affinity towards reproductive organs during pregnancy and may have potential to adversely affect reproductive processes. See 9.4.7 (Rani et al., 1992)

Breast feeding

Concentrations of chlordane in the milk of women in various populations have been reported. Restrictions on the use of the organochlorine insecticides (DDT, aldrin, dieldrin, heptachlor and chlordane) have resulted in reduced concentrations of these chemicals in breast milk and adipose tissue as compared with previous studies. The concentration of chlordane in

breast milk did not pose a hazard to breast fed infants (Stevens et al., 1993).

In one study of 1436 women residing in the United States chlordane was not found in any of the samples, and its metabolite oxychlordane was found above the detection limit (95.8 ppb) in 74% of the samples (Savage et al., 1981).

9.5 Other

No data available

9.6 Summary

10. MANAGEMENT

10.1 General principles

The condition of the patient in a particular case is decisive whether the first attention should be given to removal of the poison or to sedation of the patient.

Treatment is symptomatic, aimed at controlling convulsions, coma, and respiratory depression.

Cardiovascular function needs to be observed. If chlordane has been ingested less than one hour ago, gastric lavage after endotracheal intubation may be indicated, followed by activated charcoal slurry.

Opiates should only be administered with extreme caution because of their depressive effects on the respiratory centre. *Adrenaline* and *nor-adrenaline* should only be administered with extreme caution, because they may sensitise the myocardium and thus provoke serious cardiac arrhythmias. *Aminophylline, atropine* or *oily laxatives* should not be administered.

10.2 Life supportive procedures and symptomatic/specific treatment

Make a proper assessment of airway, breathing, circulation and neurological status of the patient.

Monitor vital signs.

Maintain a clear airway. Support ventilation using appropriate mechanical device. Administer oxygen.

Open and maintain at least one IV route. Administer IV fluids if necessary.

To control convulsions use clonazepam IV or diazepam IV or per rectum. Intravenous barbituratesmay also be used.Once convulsions are controlled further treatment with *Phenytoin* or *Sodium Valproate* should be continued for a further two to four weeks. (See the Treatment Guide on Convulsions).

Monitor blood pressure and ECG. Control cardiac dysrrhythmias with proper drug regimen and/or electrophysiologic procedures

If the patient has vomited spontaneously monitor respiratory functions and watch for signs of pulmonary aspiration.

10.3 Decontamination

Skin contact:
Remove and discard contaminated clothing. Wash exposed skin, including hair and nails with (soap and) copious amounts of water.

Eye contact:
Irrigate exposed eyes with copious amounts of water,or saline. Saline is preferable but do not delay the irrigation if only water is readily available.

Ingestion:
Inducing vomiting is contraindicated because of the risk of abrupt onset of seizures. If the patient is conscious perform gastric lavage for large ingestion, avoiding aspiration into the lungs. This should be followed by intragastric administration of a large amount of activated charcoal slurry, containing 50 to 200g of powder . Do not give fats, oils or milk, as these will enhance poison absorption from the intestinal tract.

Gastric lavage is indicated if patient is seen within one hour after ingestion.

In the case of ingestion of a solution, or an emulsifiable concentrate, a risk of chemical pneumonitis following aspiration exists.

10.4 Enhanced Elimination

Enhanced elimination is not indicated because of the large volume of distribution of chlorinated hydrocarbon insecticides.

10.5 Antidote treatment

10.5.1 Adults

There is no specific antidote

10.5.2 Children

There is no specific antidote.

10.6 Management discussion

The use of activated charcoal in the treatment of an acute chlordane intoxication is fully established. Repeated

dosing may be beneficial as it partially interrupts the entero-hepatic circulation (Hayes & Laws, 1991).

Clonazepam or diazepam are the drugs of first choice, but barbiturates also may be helpful, administered slowly by intravenous or intramuscular injection e.g. phenobarbitone (Shell Agriculture, 1990). Major side effects of the treatment with barbiturates are sedation, respiratory depression, hypotension, shock, apnoea and laryngospasm (KNMP, 1996).

When convulsions are under control and do not recur, it is recommended that treatment be continued with regular antiepileptic drugs such as *phenytoin or sodium valproate*, as required. (Shell Agriculture, 1990).

11. ILLUSTRATIVE CASES

11.1 Case reports from literature

After a 21-month-old child who had a typical convulsion following ingestion of an unknown number of chlordane "pellet" was essentially recovered, she was found to have albuminuria, and a positive urine culture; to what extend chlordane may have influenced the renal tract infection was unclear (Canada, 1962)

A woman working at a formulating plant who accidentally spilled a solution of chlordane and DDT on her belly and thighs became confused and suddenly began having convulsions after 40 minutes. She was dead before she was taken to the physician's office (Derbes, 1955).

One 30-year-old woman was exposed to chlordane by careless handling and overuse over a 1 to 4 week period. Myoclonic jerks occurred only after a delay of a month, although the patient previously suffered from circumoral numbness, anorexia, nausea and fatigue. Fatigue and anorexia became the dominant symptoms for 6 months before treatment (Garretson et al., 1985).

12. Additional information

12.1 Specific preventive measures

Rescuers must take precautions not to contaminate themselves.

The manufacture of chlordane has ceased in many countries. Disposal of any remaining stocks should be done with care to avoid contamination of the environment. Disposal can be done by burning the remaining stock in a proper incinerator designed for chlorinated hydrocarbon insecticide waste disposal. Seek further advice from the local distributor or poisons centre.

12.2 Other

Chlordane is persistent and rather immobile in soil, this substance may be hazardous to the environment; special attention should be given to fish in tropical areas. It is strongly advised not to let the chemical enter into the environment (IPCS, CEC, 1999)

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Peer review: INTOX 12 Meeting, 7 - 11 November 2000
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See Also:
Toxicological Abbreviations
Chlordane (EHC 34, 1984)
Chlordane (HSG 13, 1988)
Chlordane (PDS)
Chlordane (FAO Meeting Report PL/1965/10/1)
Chlordane (FAO/PL:1967/M/11/1)
Chlordane (FAO/PL:1969/M/17/1)
Chlordane (AGP:1970/M/12/1)
Chlordane (WHO Pesticide Residues Series 2)
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Chlordane (Pesticide residues in food: 1984 evaluations)
Chlordane (Pesticide residues in food: 1986 evaluations Part II Toxicology)